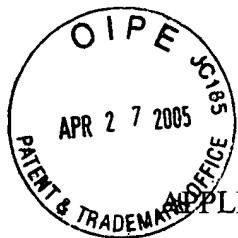


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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NUMBER: 10/773,678
FILING DATE: February 6, 2004
FIRST NAMED INVENTOR: James G. Karras
ART UNIT: 1635
EXAMINER NAME: Amy Hudson Bowman
ATTORNEY DOCKET NUMBER: ISPH-0828
TITLE: ANTISENSE OLIGONUCLEOTIDE
MODULATION OF STAT3 EXPRESSION

I certify that this communication is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Dated: 4/25/2005 By: Kemlyn Evans
Kemlyn Evans

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INFORMATION DISCLOSURE STATEMENT
Under 37 C.F.R. §§ 1.56 and 1.97-98

SIR:

Pursuant to the provisions of 37 C.F.R. §§ 1.56 and 1.97-98, enclosed herewith is PTO Form PTO/SB/08A and PTO/SB/08B listing references for consideration by the Examiner.

The filing of this Information Disclosure Statement shall not be construed as a representation regarding the completeness of the list of references, or that inclusion of a reference in this list is an admission that it is prior art or is pertinent to this application, or that a search has been made, or as an admission that the information listed is, or may be considered to be, material to patentability, or that no other material information exists, and shall not be construed as an admission against interest in any manner.

This Information Disclosure Statement is being filed:

- ☒ within three months of the filing date of the application, or date of entry into the national stage of an international application, or before the mailing date of a first office action on the merits, whichever event last occurred;
- ☐ before the mailing of a first official action after filing of a request for continued examination (RCE) under 37 C.F.R. § 1.114;
- ☐ after three months of the filing date of this national application or the date of entry of the national stage in an international application, or after the mailing date of the first official action on the merits, whichever event last occurred, but before that mailing date of the first office action to occur of either: (1) a final action under 37 C.F.R. § 1.113; or (2) an action that otherwise closes prosecution in the application, and:
- ☐ attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR
- ☐ Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:
- ☐ each item of the information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement;
- OR
- ☐ no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement.
- ☐ on or before the payment of the issue fee but after the mailing date of the first to occur of either: (1) a final action under 37 C.F.R. § 1.113; (2) a notice of allowance under 37 C.F.R. § 1.311; or (3) an action that otherwise closes prosecution in the application, and:

☐ Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

☐ each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement;

OR

☐ no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement. AND

☐ attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR

☐ after the payment of the issue fee. Applicant requests that the information contained in this Information Disclosure Statement be placed in the file according to 37 C.F.R. § 1.97(i), although the information may not be considered by the USPTO.

☒ Enclosed is a copy of each listed reference that may be material to the examination of this application, and for which there may be a duty to disclose.

☐ This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior application No. _____, filed on _____, and the references cited therein are hereby referenced, but are not required to be provided in this application under 37 C.F.R. § 1.98(d).

☒ This application was filed after June 30, 2003. Therefore, pursuant to the waiver of the requirements under 37 C.F.R. § 1.98(a)(2)(i), copies of each U.S. Patent and each U.S. Patent Application Publication are not required to be submitted. Copies of any foreign patent documents and non-patent literature cited herein are enclosed.

☐ Each item of information contained in this Information Disclosure Statement was cited in the communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this Information Disclosure Statement 37 C.F.R. § 1.704(d).

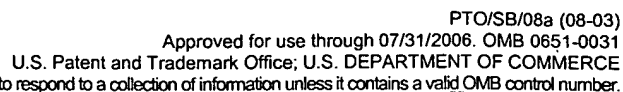
☒ Applicant submits that no fee is required for the consideration of this Information Disclosure Statement. However, if a fee is due, the Commissioner is hereby authorized to charge Deposit Account No 500252 referencing case number ISPH-0828. Consideration of the listed references and favorable action are solicited.

Respectfully Submitted,



Colleen J. McKiernan
Registration No.: 48,570
Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008

Dated: April 25, 2005

**Complete if Known**

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|-------------------------------|-------------------|
| <i>Application Number</i> | 10/773,678 |
| <i>Filing Date</i> | February 6, 2004 |
| <i>First Named Inventor</i> | James G. Karras |
| <i>Art Unit</i> | 1635 |
| <i>Examiner Name</i> | Amy Hudson Bowman |
| <i>Attorney Docket Number</i> | ISPH-0828 |

(Use as many sheets as necessary)

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| Sheet | 1 | of | 3 |
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[illegible][illegible]Date
Considered

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This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 2 of 3

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| | |
|------------------------|-------------------|
| Application Number | 10/773,678 |
| Filing Date | February 6, 2004 |
| First Named Inventor | James G. Karras |
| Art Unit | 1635 |
| Examiner Name | Amy Hudson Bowman |
| Attorney Docket Number | ISPH-0828 |

NON PATENT LITERATURE DOCUMENTS

| Examiner Initials * | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|---------------------|-----------------------|---|----------------|
| | AE | AGRAWAL, S., "Antisense oligonucleotides: towards clinical trials," <i>TIBTECH</i> (1996) 14(10):376-387. | |
| | AF | BARTON, B. E. et al., "Signal transducer and activator of transcription 3 (STAT3) activation in prostate cancer: Direct STAT3 inhibition induces apoptosis in prostate cancer lines," <i>Mol. Cancer Ther.</i> (2004) 3(1): 11-20. | |
| | AG | BRAASCH, D. A. et al., "Novel Antisense and Peptide Nucleic Acid Strategies for Controlling Gene Expression," <i>Biochem.</i> (2002) 41(14): 4503-4510. | |
| | AH | BRANCH, A. D., "A good antisense molecule is hard to find," <i>TIBS</i> (1998) 23(2): 45-50. | |
| | AI | EPLING-BURNETTE, P. K. et al., "Inhibition of STAT3 signaling leads to apoptosis of leukemic large granular lymphocytes and decreased Mcl-1 expression," <i>J. Clin. Invest.</i> (2001) 107(3): 351-361. | |
| | AJ | GEWIRTZ, A. M. et al., "Facilitating oligonucleotide delivery: Helping antisense deliver on its promist," <i>Proc. Natl. Acad. Sci. USA</i> (1996) 93: 3161-3163. | |
| | AK | GRANDIS, J. R. et al., "Requirement of Stat3 but not Stat1 Activation for Epidermal Growth Factor Receptor-mediated Cell Growth In Vitro," <i>J. Clin. Invest.</i> (1998) 102(7): 1385-1392. | |
| | AL | KARRAS, J. G. et al., "STAT3 Regulates the Growth and Immunoglobulin Production of BCL ₁ B Cell Lymphoma through Control of Cell Cycle Progression," <i>Cell. Immunol.</i> (2000) 202:124-135. | |
| | AM | LAMY, T. et al., "Dysregulation of CD95/CD95 Ligand-Apoptotic Pathway in CD3 ⁺ Large Granular Lymphocyte Leukemia," <i>Blood</i> (1998) 92(12): 4771-4777. | |
| | AN | LIU, H. et al., "Serine phosphorylation of STATE3 is essential for Mcl-1 expression and macrophage survival," <i>Blood</i> (2003) 102(1): 344-352. | |
| | AO | MAHBOUBI, K. et al., "Desensitization of Signaling by Oncostatin M in Human Vascular Cells Involves Cytoplasmic Tyr Residue 759 in gp130 but Is Not Mediated by Either Src Homology 2 Domain-containing Tyrosine Phosphatase 2 or Suppressor of Cytokine Signaling 3," <i>J. Biol. Chem.</i> (2003) 278(27): 25014-25023. | |
| | AP | MORA, L. B. et al., "Constitutive Activation of Stat3 in Human Prostate Tumors and Cell Lines: Direct Inhibition of Stat3 Signaling Induces Apoptosis of Prostate Cancer Cells," <i>Cancer Res.</i> (2002) 62(22): 6659-6666 | |

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|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Sheet 3 of 3

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| Examiner Name | Amy Hudson Bowman |
| Attorney Docket Number | ISPH-0828 |

NON PATENT LITERATURE DOCUMENTS

| Examiner Initials * | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|------------------------|--------------------------|---|----------------|
| | AQ | NIU, G. et al., "Gene Therapy with Dominant-negative Stat3 Suppresses Growth of the Murine Melanoma B16 Tumor <i>in Vivo</i> ," <i>Cancer Res.</i> (1999) 59: 5059-5063. | |
| | AR | NIU, G. et al., "Constitutive Stat3 activity up-regulates VEGF expression and tumor angiogenesis," <i>Oncogene</i> (2002) 21(13): 2000-2008. | |
| | AS | SONG, L. et al., "Activation of Stat3 by receptor tyrosine kinases and cytokines regulates survival in human non-small cell carcinoma cells," <i>Oncogene</i> (2003) 22(27): 4150-4165. | |
| | AT | TAMM, I. et al., "Antisense therapy in oncology: new hope for an old idea?" <i>Lancet</i> (2001) 358: 489-497. | |
| | AU | CHIN, ANDREW "On the Preparation and Utilization of Isolated and Purified Oligonucleotides." Document purportedly located on a CD-ROM and contributed to the public collection of the Katherine R. Everett Law Library of the University of North Carolina on March 14, 2002. | |
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Examiner
SignatureDate
Considered

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